

REMARKS

Claims 3 and 8 have been amended to more clearly describe Applicants' invention. Claim 9 has been amended to correct a clerical error. Claims 36 and 53 have been canceled without prejudice. New claim 56 has been added (support can be found, for example, at page 7, lines 16-19 of the specification). No new matter has been added. Claims 3, 4, 6, 8-12, 14, 30-35, 37-52 and 54 are pending. Claim 3, 8, 39, 49 to 52 and 54 are independent.

Objections

Claims 36 and 53 have been canceled. Applicants respectfully request withdrawal of the objections noted at pages 2 and 3 of the Action.

Rejections under 35 U.S.C. § 103(a)

Jakupovic combined with Bussey

Claims 3, 4, 6, 34-36, 39, 41, 42, 45-47 and 49-55 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over WO 96/32095 to Jakupovic et al. ("Jakupovic") combined with Bussey et al. ("Bussey"). See pages 3 to 6 of the Action. Claims 4, 6, 34-35, 41, 42, and 45-47 depend from independent claims 3, 39, 49 to 52 and 54 (claims 36 and 53 have been canceled).

The Examiner contends:

JAKUPOVIC does not teach a sterile product. The reference further does not teach the percentage by weight of the glucocorticosteroid.

BUSSEY teaches the sterilization of (gluco)corticosteroid powders by ⁶⁰Co irradiation. See entire reference, particularly the abstract. The claim also teaches that ethylene oxide is used to sterilize bulk steroids. See introduction.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to sterilize the respirable, dry powders disclosed by JAKUPOVIC by either irradiation or treatment with ethylene oxide. The artisan would have been motivated to sterilize the respirable particles to prevent microbial growth in the packaged material with a reasonable expectation of success. The artisan would be particularly

motivated to sterilize the glucocorticosteroid in the form which it is intended to be used." Page 4 of the Action.

Independent claims 3, 49, 50 and 52 and claims that depend therefrom

Applicants have discovered a pharmaceutically acceptable inhalation powder is in the form of dry, finely divided heat sterilized particles that include a glucocorticosteroid (in some examples, budesonide, rofleponide or rofleponide palmitate). See amended independent claims 3, 49, 50 and 52.

As noted by the Examiner, Jakopovic "does not teach a sterile product". Bussey does not teach or suggest a pharmaceutically acceptable inhalation powder in the form of dry, finely divided heat sterilized particles that include a glucocorticosteroid. Nothing in Jakupovic teaches or suggests an inhalation powder in the form of dry, finely divided heat sterilized particles. Jakupovic does not provide any motivation include heat sterilized particles in an inhalation powder. Bussey does not teach or suggest an inhalation powder in the form of dry, finely divided heat sterilized particles. While Bussey teaches sterilization by ⁶⁰Co irradiation or treatment with epoxy, Bussey does not provide any motivation to include sterilize particles in an inhalation powder by any method. Specifically, Bussey does not suggest or provide motivation to include heat sterilized particles in an inhalation powder. There is no motivation to combine the teachings of these references.

The motivation the Examiner refers to is not related to the teachings of either reference. Obviousness cannot be established simply by stitching together pieces of prior art using the patent as a template. Interconnect Planning Corp. v. Feil, 774 F.2d 1132, 1143 (Fed. Cir. 1985); see also Loctite Corp. v. Ultraseal Ltd., 781 F.2d 861, 873 (Fed. Cir. 1985) (denouncing courts' tendency to depart from proper standard of nonobviousness "to the tempting but forbidden zone of hindsight."); In re Fine, 837 F.2d 1071, 1075 (Fed. Cir. 1988) ("One cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention."); In re Dembiczak, 175 F.3d 994, 999 (Fed. Cir. 1999) ("Our case law makes clear that the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching or

motivation to combine prior art references.”). The cited references must provide some suggestion, motivation, or teaching for combining known components. See Heidelberg Druckmaschinen AG v. Hantscho Commercial Prods., Inc., 21 F.3d 1068, 1072, 30 USPQ2d 1377, 1379 (Fed.Cir.1994) (“When the patented invention is made by combining known components to achieve a new system, the prior art must provide a suggestion or motivation to make such a combination.”); C.R. Bard, Inc. v. M3 Systems, Inc., 157 F.3d 1340 (Fed. Cir. 2000). The requisite motivation to combine the references has not been provided. Thus, the Examiner has not presented a *prima facie* case of obviousness of claims 3, 49, 50, and 52 over Jakupovic combined with Bussey.

Even if the teachings of Jakupovic and Bussey could be properly combined, which Applicants contend is improper, this combination does not teach or suggest an inhalation powder in the form of dry, finely divided heat sterilized particles. Neither reference provides any motivation to include heat sterilized particles in an inhalation powder.

The Examiner states that “[t]he examiner agrees that the art of record would not teach a *process* to heat sterilize an inhalation powder. However, the claims are drawn to products which comprise a product-by-process, and determination of patentability is based on the product itself. *The patentability of a product does not depend on its method of production*” (page 5 of the Action, emphasis in original). As noted previously, claims 3, 49, 50 and 52 are pure product claims, not product-by-process claims. As noted by the Court of Appeals for the Federal Circuit, pure product claims when the “limitation, read in context, describes the product more by its structure than by the process used to obtain it.” Hazani v. U.S. International Trade Commission, 126 F.3d 1473, 44 USPQ.2d 1358, 1363 (Fed. Cir. 1997). In Hazani, claims reciting a “chemically engraved” surface were determined to be pure product claims, not product-by-process claims. The circumstances in Hazani closely resemble those of Applicants' claims.

An inhalation powder in the form dry, finely divided heat sterilized particles describes the structure of the product. In general, Applicants describe a heat sterilized particle including a glucocorticosteroid which has “the same pharmacological activity and physico-chemical properties/its chemical purity and physical form as the starting material from which it is

prepared, i.e. the degradation, and especially the chemical degradation." Page 7, lines 16-19 of the specification. As noted in an example in the specification, "the budosenide content has decreased by 0.5 to 4.6 percent, when exposed to β - or γ -irradiation." Page 19, lines 9-10 of the specification. See also Table 8. Structurally, the heat sterilized particle contains higher purity glucocorticosteroid and fewer degradation products than irradiation sterilized glucocorticosteroid. Thus, claims 3, 49, 50 and 52 do not describe a product-by-process, as alleged by the Examiner.¹ Jakupovic combined with Bussey does not teach or suggest an inhalation powder is in the form of dry finely divided heat sterilized particles including a glucocorticosteroid.

Accordingly, independent claims 3, 49, 50 and 52, and claims that depend therefrom, are patentable over Jakupovic combined with Bussey.

Independent claims 39 and 51 and claims that depend therefrom

Applicants have also discovered a pharmaceutically acceptable inhalation powder in the form of finely divided particles including a glucocorticosteroid (such as budesonide, rofleponide and rofleponide palmitate) and being sterilized by heat treatment at a temperature of from 100°C to 130°C. See independent claims 39 and 51.

Jakupovic combined with Bussey does not teach or suggest an inhalation powder in the form of finely divided particles, the particles being sterilized by heat treatment. Specifically, Jakupovic combined with Bussey does not teach particles sterilized by heat treatment at a temperature from 100°C to 130°C. There is no motivation in the teachings of Jakupovic or Bussey to include motivate one of ordinary skill in the art include finely divided particles, the particles being sterilized by heat treatment, in an inhalation powder. There is no motivation to combine the teachings of Jakupovic with the teachings of Bussey, or the teachings of Bussey with the teachings of Jakupovic. Thus, the Examiner has not presented a *prima facie* case of obviousness of claims 39 and 51 over Jakupovic combined with Bussey.

¹ As presented previously, Applicants' specification does demonstrate that glucocorticosteroid that has been heat treated unexpectedly contains fewer degradation products than a glucocorticosteroid sterilized by irradiation.

Accordingly, independent claims 39 and 51, and claims that depend therefrom, are patentable over Jakupovic combined with Bussey.

Independent claim 54

Applicants have also discovered pharmaceutically acceptable suspension including sterilized, finely divided particles including budesonide, rofleponide or rofleponide palmitate. See independent claim 54. Neither Jakupovic nor Bussey does not teach or suggest a suspension including sterilized, finely divided particles including budesonide, rofleponide or rofleponide palmitate. Jakupovic does not describe or suggest a suspension including sterilized, finely divided particles including budesonide, rofleponide or rofleponide palmitate. Bussey describes the ⁶⁰Co irradiation of hydrocortisone acetate, isoflupredone acetate, methylprednisolone acetate and prednisolone hydrous. See Table III on page 54 of Bussey. Neither Jakupovic or Bussey teach or suggest a pharmaceutically acceptable suspension including sterilized, finely divided particles including budesonide, rofleponide or rofleponide palmitate, or provide motivation to do so.

Accordingly, independent claim 54 is patentable over Jakupovic combined with Bussey. Applicants respectfully request reconsideration and withdrawal of these rejections.

Jakupovic combined with Bussey further combined with Sequiera or Radhakrishnan

In the Office Action, the Examiner has rejected:

(I) Claims 8-12, 14, 30, 31, 43, 44, 48, 53 and 54 under 35 U.S.C. § 103(a) as being unpatentable over Jakupovic combined with Bussey and U.S. Patent 5,837,699 to Sequiera ("Sequiera") (page 6 of Action);

(II) Claims 32, 33 and 40 under 35 U.S.C. § 103(a) as being unpatentable over Jakupovic combined with Bussey and U.S. Patent No. 5,192,528 to Radhakrishnan ("Radhakrishnan") (page 8 of the Action);

and

(III) Claims 8, 11 and 37 under 35 U.S.C. § 103(a) as being unpatentable over Jakupovic combined with Bussey, Sequiera and Radhakrishnan (page 9 of the Action).

Claims 8-12, 14, 30-33, 37, 43, 44, 48, 53 and 54 depend from independent claims 3, 8, and 54. Claims 3 and 8 feature a pharmaceutically acceptable inhalation powder in the form of finely divided heat sterilized particles including a glucocorticosteroid. Claim 54 features a pharmaceutically acceptable suspension including sterilized, finely divided particles including budesonide, rofleponide or rofleponide palmitate.

As discussed above, neither Jakupovic nor Bussey teach or suggest an inhalation powder in the form of finely divided heat sterilized particles including a glucocorticosteroid or pharmaceutically acceptable suspension including sterilized, finely divided particles including budesonide, rofleponide or rofleponide palmitate. See independent claim 3.

Neither Radhakrishnan nor Sequiera cure the deficiencies of Jakupovic or Bussey. Specifically, Radhakrishnan discloses an aqueous liposome suspension. See abstract of Radhakrishnan. Radhakrishnan does not describe an inhalation powder or a suspension of sterilized particles including budesonide, rofleponide or rofleponide palmitate. Sequiera teaches "treating of corticosteroid-responsive diseases of the upper and lower airway passages and lungs, such as asthma, by orally or intranasally administering to said passages and lungs an amount of mometasone furoate." See col. 1, lines 19-23 of Sequiera. Sequiera does not describe an inhalation powder or a suspension of sterilized particles including budesonide, rofleponide or rofleponide palmitate.

Radhakrishnan or Sequiera do not teach or suggest an inhalation powder is in the form of finely divided heat sterilized particles, or a suspension of sterilized particles including budesonide, rofleponide or rofleponide palmitate. Thus, the deficiencies of Jakupovic combined with Bussey are not cured by either Radhakrishnan or Sequiera. Indeed, a *prima facie* case alleging that these references teach the independent features of claims 3, 8, and 54 has not been presented.

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For at least these reasons, independent claims 3, 8, and 54, and claims that depend therefrom are patentable over Jakupovic combined with Bussey, Radhakrishnan and Sequiera.

Applicants respectfully request reconsideration and withdrawal of this rejection.

CONCLUSION

Enclosed is a check for the Petition for Extension of Time fee. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

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